

## PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)

<p>Date of mailing (day/month/year) see form PCT/ISA/210 (second sheet)</p>		
<p>Applicant's or agent's file reference see form PCT/ISA/220</p>		<p><b>FOR FURTHER ACTION</b> See paragraph 2 below</p>
International application No. PCT/EP2005/001939	International filing date (day/month/year) 21.02.2005	Priority date (day/month/year) 23.02.2004
<p>International Patent Classification (IPC) or both national classification and IPC C07D239/42, C07D401/12, A61K31/505, A61P29/00</p>		
<p>Applicant GLAXO GROUP LIMITED</p>		

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or Industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the International application
- Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for International preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

<p>Name and mailing address of the ISA:</p> <p> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx; 523656 epmu d Fax: +49 89 2399 - 4465</p>	<p>Authorized Officer</p> <p>Lauro, P</p> <p>Telephone No. +49 89 2399-8288</p> <p></p>
---	--

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/EP2005/001939**Box No. I Basis of the opinion**

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - a sequence listing
    - table(s) related to the sequence listing
  - b. format of material:
    - in written format
    - in computer readable form
  - c. time of filing/furnishing:
    - contained in the international application as filed.
    - filed together with the international application in computer readable form.
    - furnished subsequently to this Authority for the purposes of search.
3.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/EP2005/001939**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or  
industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Yes: Claims	1-10
	No: Claims	
Inventive step (IS)	Yes: Claims	1-10
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-8,10
	No: Claims	9

**2. Citations and explanations****see separate sheet****Box No. VI Certain documents cited**

1. Certain published documents (Rules 43bis.1 and 70.10)  
and / or
2. Non-written disclosures (Rules 43bis.1 and 70.9)

**see form 210**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2005/001939

**Re Item V.**

**1 Reference is made to the following documents:**

D1 : WO 00/39101 A (ASTRAZENECA UK LIMITED; BRADBURY, ROBERT, HUGH; BREAULT, GLORIA, ANNE;) 6 July 2000 (2000-07-06)

D2 : WO 97/09315 A (SIGNAL PHARMACEUTICALS, INC; SUTO, MARK, J; GOLDMAN, MARK, E; GAYO, LE) 13 March 1997 (1997-03-13)

D3: WO 2004/018434 A (GLAXO GROUP LIMITED; EATHERTON, ANDREW, JOHN; GIBLIN, GERARD, MARTIN,) 4 March 2004 (2004-03-04)

**2 Document D3, which was published after the priority date of the current application is not taken into account for the purposes of the present opinion.**

**3. Novelty**

The compounds of the present application differ from the structurally closest compounds of the prior art, which are disclosed in D1, in the nature of the group represented by R6 in formula (I) of the present application. Novelty is therefore acknowledged.

**4. Inventive step**

The problem underlying the present application appears to reside in the provision of pyrimidine derivatives useful in the treatment of diseases which are caused directly or indirectly by an increase or decrease in activity of the cannabinoid receptor.

Anti-inflammatory agents which acts as cytokine inhibitors are disclosed in D2; however, since no mention is to be found in D2 that the compounds also modulate the cannabinoid receptor, the qualitative activity of the compounds of the present application is considered as being unexpected in view of D2 and an inventive step can be acknowledged.

**5. Industrial applicability**

Claim 9 is directed to a method for treatment of the human or animal body by

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2005/001939

therapy.

**6. Further observations:**

- For the "optionally substituted" substituents in claim 1, a list of the suitable substituents should be inserted in the claim.
- Claim 6 contains an unallowable reference to the description.